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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,315	11/05/2001	Alison F. Chalker	GM50049	6943

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SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER

JOHANNSEN, DIANA B

ART UNIT PAPER NUMBER

1634

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,315	CHALKER ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 and 24-32 is/are rejected.
- 7) ☒ Claim(s) 13,28 and 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1101</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. This application is a 371 of PCT/US00/12103, filed May 4, 2000. It is noted that the International Search Report and International Preliminary Examination Report for PCT/US00/12103 have been received and considered.
2. It is also noted that the paper and computer readable forms of the Sequence Listing filed November 5, 2001 have been entered.

Election/Restriction

3. Applicant's election without traverse of Group I, claims 1-22 and 24-32, in the Response filed June 6, 2003 is acknowledged.
4. Claim 23 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the Response of June 6, 2003.

Priority

5. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

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6. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

7. The disclosure and claims 13 and 28-29 are objected to because of the following informalities: in both the specification and the claims (particularly claims 13 and 28-29) degrees Celsius are abbreviated as "EC" rather than by a standard, art-recognized abbreviation such as "°C". Upon conducting an internet search, the examiner determined that the standard abbreviation "°C" may be depicted as "EC" by software that does not recognize and convert the degree symbol correctly. Appropriate correction of this obvious typographical error is required.

8. The disclosure is objected to because of the following informalities: the disclosure includes a description of "Figure 1" (see page 4); however, no Figures were filed with the instant application.

Appropriate correction is required.

9. The use of the trademark AMPLITAQ® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-22 and 24-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-22 are indefinite over the recitation of the phrase "site in the molecule targeted for disruption" in claim 1, step (a), and further over the subsequent recitation of the limitation "the target site." First, it is unclear from the language "site in the molecule targeted for disruption" as to whether it is the site or the molecule that is intended to be modified by the recitation "targeted for disruption" (i.e., does this language refer to a particular site within a molecule, wherein that molecule is targeted, or is this language intended to refer to a particular site that is "targeted"?). Further, as the claim does not previously recite or refer clearly to a "target site," there is insufficient antecedent basis in the claims for the recitation "the target site."

Claims 1-22 are indefinite over the recitation of the limitation “the amplification” in step (a) because there is insufficient antecedent basis for this limitation in the claims. This rejection could be overcome by amending the claim to recite “the amplifying” or “said amplifying.”

Claims 1-22 are indefinite over the recitation of the limitation “mixing the first and second fusion products of (c) and (e) and amplifying the fusion products via polymerase chain reaction, thereby producing a nucleic acid cassette fusion....” in step (f) of claim 1. While it is clear that the claimed method requires production of the recited “nucleic acid cassette fusion,” the recitation “mixing the first and second fusion products of (c) and (e) and amplifying the fusion products via polymerase chain reaction” does not make clear what steps or actions actually occur to produce the cassette fusion. Particularly, it is unclear as to whether the claim is intended to require separate steps of mixing products and amplifying those same products by PCR (as the language of the claim seems to suggest), or whether this language is intended to require that, e.g., the mixture formed by mixing the first and second fusion products is subsequently subjected to PCR. Clarification is required.

Claims 3-6 are indefinite over the recitation of the limitation “the amplification step (a)” in claim 3 because there is insufficient antecedent basis for this limitation in the claims. This rejection could be overcome by amending the claim to recite, e.g., “the amplifying of step (a).”

Claims 3-6 are indefinite over the recitation of the limitation "the region upstream of the target site" in claim 3 because there is insufficient antecedent basis for this limitation in the claims.

Claims 7-9 are indefinite because while the claims describe a "second set of primers, P3 and P4," the claims do not previously refer to, e.g., a first set of primers. Accordingly, it is unclear as to whether the claims are intended to require one or two sets of primers. This rejection could be overcome by amending claim 7 such that it depends from a claim that does refer to a first set of primers, such as claim 3.

Claims 7-9 are indefinite over the recitation of the limitation "the amplification step (a)" in claim 7 because there is insufficient antecedent basis for this limitation in the claims. This rejection could be overcome by amending the claim to recite, e.g., "the amplifying of step (a)."

Claims 7-9 are indefinite over the recitation of the limitation "the forward primer" and "the reverse primer" in claim 7 because there is insufficient antecedent basis for this limitation in the claims.

Claims 7-9 are indefinite over the recitation of the limitation "the region downstream of the target site" in claim 7 because there is insufficient antecedent basis for this limitation in the claims.

Claims 7-9 are indefinite over the recitation of the limitation "the 3' end of the cassette" in claim 7. While claim 1 previously refers to the 3' end of a "first strand" of the cassette, the claim does not previously refer to a "3' end of the cassette." Accordingly, there is insufficient antecedent basis for this limitation.

Claim 10 is indefinite over the recitation of the limitation “amplifying the cassette prior to mixture with the amplification products of (c) or (e).” It is noted that steps (c) and (e) are drawn to steps of “amplifying” (whereas steps (b) and (d) are drawn to “mixing”). It is unclear as to how the recited requirement for “amplifying the cassette prior to mixture” is intended to further limit steps (c) and (e), as mixing has already occurred at these stages of the method. Clarification is required.

Claim 11 is indefinite over the recitation of the limitation “the amplification step (c)” because there is insufficient antecedent basis for this limitation in the claims. This rejection could be overcome by amending the claim to recite, e.g., “the amplifying of step (c).”

Claim 11 is indefinite over the recitation of the limitations “the forward primer” and “the region upstream of the target site” because there is insufficient antecedent basis for these limitations in the claims.

Claim 12 is indefinite over the recitation of the limitation “the amplification step (d)” because there is insufficient antecedent basis for this limitation in the claims. It is noted that step (d) is a step of “mixing.”

Claim 12 is indefinite over the recitation of the limitations “the forward primer,” “the reverse primer,” and “the region downstream of the target site” because there is insufficient antecedent basis for these limitations in the claims.

Claims 13-14 are indefinite over the recitation of the limitation “the amplification of (f)” in claim 13 because there is insufficient antecedent basis for this limitation in the

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claims. This rejection could be overcome by amending the claim to recite, e.g., "the amplifying of (f)."

Claims 13-14 are indefinite over the recitation of the limitations "the mixture of (f)," "the heated mixture of (g)," and "the nucleotide sequences downstream of the target site (a)" in claim 13 because there is insufficient antecedent basis for these limitations in the claims.

Claims 21-22 are indefinite over the recitation of the limitation "said nucleic acid sequences" because there is insufficient antecedent basis for this limitation in the claims.

Claims 24-28 are indefinite because it is unclear as to whether the claims are intended to be drawn to a method for producing a "nucleic acid-cassette fusion" as recited in the preamble of claim 24, or to a method for producing a "DNA sequence fusion cassette" as recited in the final method step. Further, it is unclear as to whether the recitation "DNA" in the term "DNA sequence fusion cassette" in step (e) is intended to be further limiting, such that any product produced by the method must consist entirely of DNA. Clarification is required.

Claims 24-28 are indefinite over the recitation of the limitation "the target site" in claim 24, step (a), because there is insufficient antecedent basis for this limitation in the claims.

Claims 24-28 are indefinite over the recitation of the limitation "said first and second region comprising a first strand having a first and second end." It is unclear as to whether this language requires that "said first and second region" of the selected

DNA molecule comprise a single "first strand" that has first and second ends, or whether this language requires that each of said first and second region comprises a first strand (which first strand has first and second ends). Clarification is required.

Claims 24-28 are indefinite over the recitation of the limitations "the second end of the first region" and "the first end of the second region" in claim 24, step (b), because there is insufficient antecedent basis for this limitation in the claims. While claim 24 previously recites the limitation "said first and second region comprising a first strand having a first and second end," the claim does not previously refer to a "second end of the first region" or a "first end of the second region."

Claims 24-28 are indefinite over the recitation of the limitation "amplifying the selected DNA sequence using primers for the first and second region, thereby producing amplified first and second regions." First, there is insufficient antecedent basis for the limitation "the selected DNA sequence." Second, it is unclear as to whether this language requires amplification to produce a single product comprising the first and second regions, or whether this recitation is intended to refer to separate amplification of the first region and the second region (to produce an amplified first region and an amplified second region). Clarification is required.

Claims 24-28 are indefinite over the recitation of the limitation "the DNA sequence" in claim 24, step (e) because there is insufficient antecedent basis for this limitation in the claims. It is unclear as to whether this recitation is intended to refer back to, e.g., the "selected DNA molecule" of (a) or the "selected DNA sequence" of (c), or to refer to some other "DNA sequence." Clarification is required.

Claim 25 is indefinite over the recitation of the limitations “the primers for the ends of the first and second regions which overlap with the ends of the cassette” and “the sequences of the overlap” because there is insufficient antecedent basis for these limitations in the claims. Further, as claim 24 recites more than one “overlap,” it is unclear as to which of these might constitute “the overlap” of claim 25.

Claim 28 is indefinite over the recitation of the limitation “the nucleotide sequence region downstream of the target site” because there is insufficient antecedent basis for this limitation in the claims.

Claim 29 is indefinite because it is unclear as to whether the claim is intended to be drawn to a method for producing a “nucleic acid-cassette fusion” as recited in the preamble of the claim, or to a method for producing a “DNA sequence fusion cassette” as recited in the final method step. Further, it is unclear as to whether the recitation “DNA” in the term “DNA sequence fusion cassette” in step (k) is intended to be further limiting, such that any product produced by the method must consist entirely of DNA. Clarification is required.

Claim 29 is indefinite over the recitation of step (c). Both step (b) and step (c) are drawn to steps of mixing the cassette and the first and second regions, and therefore it is unclear as to how step (c) is intended to further limit the claimed method.

Claim 29 is indefinite over the recitation of the limitation “the heated mixture of (i)” because there is insufficient antecedent basis for this limitation in the claims.

Claim 29 is indefinite over the recitation of the limitation “the first and second regions of the DNA sequence” and “the DNA sequence” in step (k). While the claim

previously refers to a “first region of DNA sequences” and a “second region of DNA sequences, the claim does not previously refer to a single “DNA sequence” or regions thereof.

Claims 30-32 are indefinite over the recitation of the limitation “the target site” in claim 30, step (a), because there is insufficient antecedent basis for this limitation in the claims.

Claims 30-32 are indefinite over the recitation of the limitation “the selected Streptococcus DNA sequences” in claim 30, step (d), because there is insufficient antecedent basis for this limitation in the claims.

Claim 31 is indefinite over the recitation of the limitation “the nucleic acid sequence” because there is insufficient antecedent basis for this limitation in the claims.

Claim 32 is indefinite over the recitation of the limitation “the nucleic acid fusion molecules” because there is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 24-27 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wach (Yeast 12(3):259-265 [3/1996]).

Wach discloses a two-step PCR method for constructing a “disruption cassette” (see entire reference, particularly Figure 1, pages 261-263). In the first step of Wach’s

method, first and second regions in a target gene flanking a target site are amplified by PCR to produce amplified first and second fragments; the PCR employs primers that result in the 3' end of the first fragment being homologous to the 5' end of an antibiotic resistance marker gene, and the 5' end of the second fragment being homologous to the 3' end of that marker gene (see Figure 1, panel B, and the description thereof, and pages 262-263). These steps of Wach meet the requirements of steps (a) and (c) of the claimed method. In the second step of Wach's method, the amplified first and second fragments are combined with the marker gene, and PCR is carried out to produce fusion products comprising the marker flanked by the first and second fragment sequences (see Figure 1, panel B, and pages 262-263). These steps meet the requirements of steps (d) and (e) of the claimed method. Regarding step (b), it is noted that the marker gene employed by Wach is not disclosed as being homologous at its 5'- and/or 3'- end with the first and second regions of the target molecule; however, the claims as written encompass any type and length of "overlap;" accordingly, as any two nucleic acid molecules "overlap" by at least one nucleotide, the marker gene taught by Wach meets the requirements of the claims as written. Wach's method results in the synthesis without ligation of a fusion molecule that is both a "DNA sequence fusion cassette" and a "nucleic acid-cassette fusion," as required by the final step and preamble of the claims. Regarding claims 25-27, Wach discloses primers for the 3' end of the first region and the 5' end of the second region that overlap the ends of the marker gene by 26 nucleotides. Accordingly, Wach clearly anticipates claims 24-27.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Yeast 12(3):259-265 [3/1996]) in view of Claverys et al (Gene 164(1):123-128 [10/1995]) and Brush (The Scientist 12(20):21 [10/1998]).

Wach discloses a two-step PCR method for constructing a "disruption cassette" (see entire reference, particularly Figure 1, pages 261-263). In the first step of Wach's method, first and second regions in a target gene flanking a target site are amplified by PCR to produce amplified first and second fragments; the PCR employs primers that result in the 3' end of the first fragment being homologous to the 5' end of an antibiotic resistance marker gene, and the 5' end of the second fragment being homologous to

the 3' end of that marker gene (see Figure 1, panel B, and the description thereof, and pages 262-263). In the second step of Wach's method, the amplified first and second fragments are combined with the marker gene, and PCR is carried out to produce fusion products comprising the marker flanked by the first and second fragment sequences (see Figure 1, panel B, and pages 262-263). Regarding step (b), it is noted that the marker gene employed by Wach is not disclosed as being homologous at its 5'- and/or 3'- end with the first and second regions of the target molecule; however, the claims as written encompass any type and length of "overlap;" accordingly, as any two nucleic acid molecules "overlap" by at least one nucleotide, the marker gene taught by Wach meets the requirements of the claims as written. Wach's method results in the synthesis without ligation of a nucleic acid fusion molecule.

Wach exemplifies the use of an *S. cerevisiae* target molecule, and therefore does not teach a target nucleic acid molecule comprising *Streptococcus* DNA sequences or a fusion product that comprises first and second regions of a streptococcal DNA sequence flanking a cassette. Further, Wach does not teach a high throughput method in which PCR amplification is carried out in a "plurality of reaction wells."

Claverys et al teach that drug resistance cassettes and gene disruption cassettes comprising marker and/or reporter genes flanked by streptococcal sequences are widely used to study gene activity and pathogenesis in *S. pneumoniae* (see entire reference, particularly pages 123-124). Accordingly, in view of the teachings of Claverys et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Wach so as to have

carried out Wach's method using a streptococcal gene of interest as the target sequence and any desired antibiotic resistance gene and/or reporter gene as the marker gene. As Wach discloses that his method is "faster and more versatile compared to conventional cloning techniques" for preparing disruption cassettes useful in transforming target organisms (see page 265), an ordinary artisan would have been motivated to have made such a modification for the advantages of efficiency and versatility in preparing such molecules. Further, Brush discloses that the use of multi-well plates adapted for use with interchangeable-block thermocyclers allows for increased versatility and decreased risk of contamination in practicing PCR (see entire reference, particularly page 1/6). In view of the teachings of Brush, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method suggested by Wach and Claverys et al so as to have simultaneously carried out multiple amplification reactions in the wells of a plate for the advantages of increased efficiency, versatility, and reduced risk of contamination, as suggested by Brush.

Regarding claim 31, it is noted that Claverys et al disclose streptococcal target sequences located on plasmids (see, e.g., pages 125-126); given the availability of such plasmids containing target sequences of interest, it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to have employed such plasmids in the preparation of additional fusion cassettes for the advantages of convenience and efficiency. Regarding claim 32, both Wach and Claverys et al disclose transformation of target organisms and detection of disruption cassettes in

transformants (see Wach, page 262, right column; Claverys et al, pages 124-126). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have employed the fusion constructs suggested by Wach and Claverys et al in preparing *Streptococcus* transformants, and to have further confirmed the correct insertion of cassettes in the target gene of interest, for the advantage of rapidly preparing transformants useful in the study of streptococcal gene activity and pathogenesis, as suggested by Claverys et al.

Allowable Subject Matter

17. Regarding the invention of claims 28-29, it is noted that Wach does not disclose, e.g., a step of cooling to 50°C over about 30 minutes, or the use of multiple polymerases, as recited in the instant claims. As such steps necessitate the use of additional time and reagents, and as Wach discloses that his method may be employed successfully without such additional steps and reagents, one of ordinary skill in the art would not have been motivated to have modified the method of Wach so as to have added such steps. Regarding the invention of claims 1-22, the closest prior art reference, Zhong et al (BioTechniques 15(5):874, 876-8 [1993]), discloses a method in which an insertion cassette is amplified with primers having homology to first and second regions of a target gene, in which the amplified cassette is used to prime amplification of the first and second regions, thereby producing two fusion constructs, and in which the two fusion constructs are annealed, elongated and amplified to produce a fusion construct containing the target regions flanking the cassette (see pages 876-877, Figure 2). In contrast to Zhong et al, the claimed method requires

additional steps of separately amplifying target regions prior to conducting steps of amplifying the first and second amplification products with the cassette (and subsequently combining and amplifying the first and second fusion products). As such steps necessitate the use of additional time and reagents, and as Zhong et al disclose that their method may be employed successfully without such additional steps and reagents, one of ordinary skill in the art would not have been motivated to have modified the method of Zhong et al so as to have added such steps.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

A handwritten signature in dark ink, appearing to read "Diana B. Johannsen", followed by a long horizontal line extending to the right.

Diana B. Johannsen
August 24, 2003